

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Laura Madison, Gjalb W. Huisman and Oliver P. Peoples

Serial No.: 09/235,875 Art Unit: 1638

Filed: January 22, 1999 Examiner: Russell Kallis

For: *TRANSGENIC SYSTEMS FOR THE MANUFACTURE OF POLY(3-HYDROXY-BUTYRATE-CO-3-HYDROXYHEXANOATE)*

As discussed in the interview held March 8, 2006 with the Examiner, Dr. Peoples and the undersigned, the art cited in the Office Action mailed February 10, 2006 describes production of 3-hydroxyhexanoate containing polymers by the beta oxidation pathway by providing substrates of C6 or longer fatty acids. In contrast to the cited art, the present application discloses genetically engineering bacteria to produce of 3-hydroxyhexanoate from butyryl-CoA plus acetyl-CoA.

Rejection Under 35 U.S.C. § 102

Claims 1, 7, 16, and 18-21 were rejected under 35 U.S.C. § 102(b) as being anticipated by Fukui, et al., *J. of Bacteriol.* 179:4821-4830 (1997) ("Fukui"). Fukui discloses production of poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) by the beta oxidation pathway by providing substrates of C6 or longer fatty acids, specifically hexanoate and octanoate. The claims of the present application are drawn to production of 3-hydroxyhexanoate from butyryl-CoA plus acetyl-CoA, which is not disclosed or suggested by Fukui. Therefore, Fukui does not anticipate the claims of the present application.

Rejections Under 35 U.S.C. § 103

(i) Claims 1, 6-7, 16 and 18-21 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Fukui, in view of U.S. Patent No. 5,470,727 to Macharenas, et al. ("Macharenas") and further in view of Schubert, et al., *J. of Bacteriology* 1998, Vol. 170, No. 12, p. 5837-5847 ("Schubert"). As discussed above, the claims are drawn to production of 3-hydroxyhexanoate from butyryl-CoA and acetyl-CoA, which is not disclosed or suggested by Fukui. Macharenas and/or Schubert do not make up for this deficiency since neither reference discloses or suggests production of 3-hydroxyhexanoate from butyryl-CoA and acetyl-CoA. Therefore, the claims are not obvious.

(ii) Claims 1, 7, 10 and 18-21 were rejected under 35 U.S.C. § 103(a) as unpatentable over Timm, et al., *Applied and Environmental Microbiology*, 56(11):3360-3367 (1990) ("Timm"), in view of Fukui and further in view of Hoffmann, et al., *FEMS Microbiology Letters* 184:253-259 (2000) ("Hoffmann"). Timm discloses production of 3-hydroxyhexanoate containing polymers when octanoate is given as substrate (see page 3366, column 1, first full paragraph). Timm does not disclose or suggest production of 3-hydroxyhexanoate from butyryl-CoA and acetyl-CoA. Fukui and Hoffmann do not make up for this deficiency. Fukui also discloses production of 3-hydroxyhexanoate containing polymers from octanoate or hexanoate, not butyryl-CoA and acetyl-CoA. Hoffmann discloses production of PHAs from gluconate, not butyryl-CoA and acetyl-CoA. Timm, Fukui and Hoffmann do not disclose or suggest using butyryl-CoA and acetyl-CoA as substrates for production of polymers containing 3-hydroxyhexanoate. Therefore, the claims are not obvious.

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(iii) Claims 1, 7, 14 and 16-21 were rejected under 35 U.S.C. § 103(a) as unpatentable over Schubert, in view of Fukui and further in view of Boynton, et al., *J. of Bacteriology* 178(11):3015-3024 (1996) ("Boynton") and Feigenbaum, et al., *PNAS* 74(2):492-495 (1977) ("Feigenbaum"). Schubert discloses production of poly- β -hydroxybutyric acid (PHB) in *E. coli*. Schubert does not disclose or suggest genetically engineering bacteria to produce 3-hydroxyhexanoate containing polymers from butyryl-CoA and acetyl-CoA. Fukui, Boynton and Feigenbaum do not make up for this deficiency. As discussed above Fukui discloses use of hexanoate or octanoate as substrates for production of 3-hydroxyhexanoate containing polymers. Feigenbaum discloses isolation of a multi-enzyme complex of fatty acid oxidation from *E. coli*. Boynton discloses cloning of β -hydroxybutyryl-CoA dehydrogenase and butyryl-CoA dehydrogenase from *C. acetobutylicum*. Feigenbaum and Boynton do not disclose or suggest genetically engineering bacteria to produce 3-hydroxyhexanoate containing polymers from butyryl-CoA and acetyl-CoA. Clearly it would not be obvious to one of skill in the art how to genetically engineering bacteria to produce 3-hydroxyhexanoate containing polymers from butyryl-CoA and acetyl-CoA based on the cited art. Therefore, the claims are not obvious.

Proposed Claim Amendments

A number of amendments suggested by the examiner were presented but not entered. To the extent these overcome any remaining issues under 35 U.S.C. 112, applicants will re-present them. However, the amendments are not required to distinguish over the prior art. **None** of the prior art discloses explicitly, implicitly or inherently, the claimed method of making PHAs using the genetically engineered organisms. The prior art discloses, at most, various sources of the

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requisite genes, but not the teaching that would lead one skilled in the art to combine as applicants have done, with a reasonable expectation of success, so that the organisms can utilize inexpensive substrate to produce these polymers. An excellent discussion on these polymers, their industrial utilization, and ways in which they have been engineered to enhance production while reducing cost of production to a level that permits commercialization, can be found on the assignee's website, www.metabolix.com.

Allowance of claims 1, 6-7, 10, 14, 16-21 and 35-39 is respectfully solicited.

Respectfully submitted,

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